GENETIC RELATIONSHIPS BETWEEN SCHIZOPHRENIA AND A VISIBLE SUBPAPILLARY PLEXUS IN THE NAILFOLD

By

CHARLES EDWARD BUCHANAN

A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL OF
THE UNIVERSITY OF FLORIDA
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA
1968

ACKNOWLEDGMENTS

The author is indebted to all members of his committee for their suggestions and assistance in the development and completion of this project. Grateful acknowledgment is extended to the following: Dr. Marshall B. Jones, Chairman; Dr. Louis D. Cohen; Dr. Richard Anderson; Dr. Bruce Thomason; and Dr. Charles Vierck.

Special acknowledgment is extended to Miss Shirley L. Holstein, R.N., M.S., who did the microscopic examinations of the nailfold capillaries.

TABLE OF CONTENTS

Page

ACKNOWLEDGMENTS ii

LIST OF TABLES. v

LIST OF FIGURES vi

CHAPTER

I. INTRODUCTION 1

The Problem. 1
Theoretical Considerations 2
Genetics 6
Somatotype 15
Cardiovascular System. 19
Capillaries of the Nailfold. 21
Summary. 26
Hypotheses 30

II. EXPERIMENTAL PROCEDURE 31

Study I: In-Hospital Study. 31
Study II: Within-Family Study 40

III. RESULTS. 45

Study I: In-Hospital Study. 45
Study II: Within-Family Study 50

IV. DISCUSSION 66

V. SUMMARY. 80

Page

APPENDIX

A. PHILLIPS PROGNOSTIC RATING SCALE. 84

B. FAMILY HISTORY. 88

C. WITHIN-FAMILY INFORMATION 92

D. SCHIZOTYPE CHECK LIST WITH SCORE WEIGHTING. 98

REFERENCES. 101

BIOGRAPHICAL SKETCH 107

LIST OF TABLES

Table Page

1. Schizophrenia Rates in Twins 8

2. Personality Patterns in Identical Twins of Patients. 10

3. Means and Standard Deviations for the Plexus Rating, Age, Age of Onset, Duration of Illness, Number and Length of Hospitalizations as a Function of Family History (Positive, Negative, or No Information). . . 46

4. Within-Group Correlations between the Plexus Rating and Age, Age of Onset, Duration of Illness, Number and Length of Hospitalizations. 47

5. Means and Standard Deviations for the Plexus Rating, Age, Age of Onset, Duration of Illness, Number and Length of Hospitalizations in Male and Female Population. 48

6. Subpapillary Plexus Rating as a Function of Diagnosis 49

7. Means and Standard Deviations for Age, Plexus Ratings, and Schizotypy Ratings among the 34 Probands, Their Parents, and Their Siblings 55

8. Parental Concordance of Schizotypy and Plexus. 57

9. Parental Predominance on the Schizotypy Rating as a Function of Positive Family History. 58

10. Parental Predominance on the Plexus Rating as a Function of Positive Family History . . 60

LIST OF FIGURES

Figure Page

1. Schematic cross section of the skin 23
2. Schematic cross section of the skin as it forms the nailfold. 34
3. Schematic drawing of the different grades of subpapillary plexus. 37
4. Scatter diagram for schizotypy ratings of the probands' mothers and fathers 53
5. Schematic drawing of the folding condition. . 61
6. Folding condition 1 63
7. Folding condition 2 64

CHAPTER I

INTRODUCTION

The Problem

The central purpose of this investigation is to evaluate the relationship between a visible subpapillary plexus in the nailfold and the manifestation of schizophrenic psychopathology within the families of diagnosed schizophrenics. The subpapillary plexus is an anatomical variant which bears known relationships to schizophrenia. Capillary morphology in general has been demonstrated to be under genetic control. However, the degree to which the subpapillary plexus is visible is dependent upon both the morphology of the vasculature and the thickness of the tissue layer which comprises the vascular bed. The genetics of the subpapillary plexus per se remain to be worked out. If the plexus is found to be heritable and to be associated with the kinds of behavior pathology which characterize schizophrenia, then a study of this relationship may provide a more precise understanding of the biological factors which are associated with the development of schizophrenic reactions.

As a first step, the relationship between the subpapillary plexus and a family history of mental illness must be investigated. Second, it must be determined whether the plexus appears more frequently in those kinds of schizophrenia which historically have been held to show more constitutional factors in the presumed etiology. Third, and most important, it is necessary to know if the plexus is associated with psychopathology, per se, rather than occurring only within the context of a manifest psychotic reaction. If a plexus and the kinds of psychopathology which characterize subclinical schizophrenia are positively related, then the possibility that the plexus is an antecedent of some of the schizophrenias and has etiological significance as a component of the constitutional diathesis would be strengthened.

Theoretical Considerations

The report of the World Health Organization on the epidemiology of psychiatry states that "Hypotheses about the etiology of mental illness are so diverse as to defy incorporation into any comprehensive theory" (Tsung-Yi Lin

& Standley, 1962, p. 9). Similarly, Cumming (1961) describes the theoretical conceptions of the etiology of schizophrenia as chaotic. In an effort to bring some order into the understanding of schizophrenia, Rosenthal (1963) has constructed a three-fold classification of theories which provides the following guidelines which are helpful in making variables explicit.

In _life experience_ theories, the etiological agent is thought to be psychogenic or sociogenic. These theories are usually derived from a psychoanalytic position, and although lip service is sometimes paid to Freud's supposition that the ego has constitutional determinants, biological factors are not taken into consideration in research strategies. The disorder is thought to result from interpersonal conflict and faulty learning.

Monogenic-biochemical theories posit a mutant gene as the cause of a specific error of metabolism. This is the basic construct of genetic and biochemical research. Most but not all persons who have the genetic makeup will manifest the disorder. The lower penetrance of the gene may be caused by constitutional resistances (Kallmann, 1953). Research strategies focus on searching for the particular biochemical anomalies.

Diathesis-stress theories bear a resemblance to the monogenic-biochemical ones but with these crucial differences: For these theories, what is inherited is a constitutional predisposition to the disease; the disease will not become manifest unless the predisposition is acted upon by a stressor which is usually thought to be psychological.

Meehl (1962) has put forth a notably comprehensive diathesis-stress theory of the etiology of schizophrenia in which he argues that the concordance rates of twin studies are of such a magnitude as to represent the most important piece of etiological information that we have. Meehl holds that the mutant gene produces a schizotaxia characterized by a neural integrative deficit. Such a person, called a schizotype, may compensate on that level or develop a clinical schizophrenia, depending on the social learning history and constitutional resistances. According to Meehl, only a small percentage of schizotypic persons develop schizophrenia, but all schizotaxic people, on all current social reinforcement regimes, become, to some degree, schizotypic and exhibit characteristic behavioral deviations which at the present can be roughly quantified.

Meehl's theory contains two major points which should serve to extend diathesis-stress conceptions. First, schizotypes should have the genetic, constitutional diathesis in varying degrees, and they should occur in sizable numbers in the families of schizophrenic probands. Second, schizotypes exhibit, in subclinical form, identifiable behavior which is qualitatively similar to that characterizing manifest schizophrenia. Meehl's theory takes into consideration the ideas of constitutional defenses but does not elaborate upon them. The assumed resistance factors may be genetically distributed independently of the primary mutant gene, and their effects could combine in a complementary series to form the predisposition. At the present state of development of the theory it is not crucial to distinguish sharply between the mutant etiological gene and the resistance factors. Both participate in the diathesis. The major requirement of diathesis-stress theory at the present is to identify a genetically transmitted, constitutional variation which is characteristic of schizophrenia and which is not a function of the disease or its contingencies such as hospitalization, nutrition, drugs, and so on.

Factors resulting from the disease process have seriously hampered almost all biologic research (Kety, 1948). The lesson taught by the relative lack of success of prior physiological and biochemical studies is that a more promising research strategy would be to look for the diathesis in bodily systems which are relatively low in feedback from the disease itself. For example, the endocrine system is rich in feedback inputs, but anatomical structures should show relatively low effects. Therefore, a conservative approach would indicate that the genetic diathesis should be looked for in structures and functional systems of the body less affected by the disequilibria which accompany the psychotic reaction. This method of proceeding is compatible with diathesis-stress theories because they embody the implicit requirement that the constitutional predisposition be identifiable antecedent to the development of the schizophrenia. Subsequent sections will therefore contain a review of the evidence provided by genetics, somatotype, and the cardiovascular system, which have all shown persistent, discriminating variation in the schizophrenias.

Genetics

For many years evidence has accumulated which indicates that genetic factors are significant in the etiology of at least some of the schizophrenias (Planansky, 1955). Extensive population and twin studies have been carried out by a number of investigators in different countries which have yielded comparable results (Kallmann, 1953). Although these studies have suffered from certain methodological limitations (Rosenthal, 1962; Pastore, 1949), the general conclusions to which they point are probably sound (Hurst, 1951, 1952). Kallmann, using the twin family method, has demonstrated a strong positive relationship between concordance for schizophrenia and the degree of blood relationship within the family. Although Kallmann's concordance figures for his monozygotic twins are somewhat higher than those given by other investigators, it should be pointed out that the over-all differences which he reports in concordance between the dizygotic and monozygotic twin pairs are, according to Fuller and Thompson (1960), similar in magnitude to those given by Rosanoff, Essen-Moller, Slater, and Luxenburger. The results of these studies are summarized in Table 1. Both Kallmann and Slater have also examined the other siblings in families which contain a schizophrenic twin proband, and have found that non-twin siblings show a concordance rate of the same order of magnitude as found in dizygotic twin pairs (Planansky, 1955). Kallmann (1946) reported on the concordance of step-siblings, 1.8 percent; half-siblings, 7.0 percent; full-siblings, 14.3 percent; dizygotic twins, 14.5 percent; monozygotic twins, 86.2

TABLE 1

SCHIZOPHRENIA RATES IN TWINS

Researcher	Monozygotics		Dizygotics	
	No. of Pairs	Concordance	No. of Pairs	Concordance
		(%)		(%)
Luxenberger	17	67	33	0
Rosanoff _et al_.	41	67	101	10
Essen-Moller	7	71	24	17
Kallmann	268	86	685	15
Slater	41	76	115	14

percent. This linear relationship between degree of blood relationship and manifestation of schizophrenia provides strong evidence for a genetic component in the etiology of the disorder.

On the other hand, Tienari (1963) fails to confirm the generally high concordance rates in monozygotic twins reported by other investigators. He found 16 schizophrenic probands in 125 pairs of monozygotic twins identified by a general population survey. The co-twins of the 16 probands were all considered discordant. Karlsson (1966) criticizes this study, and states that the case histories did not fully support discordance in the co-twins. Karlsson offers the opinion that Tienari included cases of lesser severity in his probands which other investigators would have failed to designate as schizophrenic. Rosenthal (1961) gives support to this contention, and claims that index cases drawn from hospital populations tend to select for study only the more severe cases of schizophrenia. This selective factor would result in elevated concordance figures. Such an elevation of concordance figures would also apply to family incidence studies if chronicity of the disorder correlates with genetic loading in the family. Kallmann (1953) reports that this is, indeed, the case and that the catatonic and hebephrenic categories, which tend to become chronic, have a much higher familial incidence of schizophrenia. Kringlin (1966), in a recent, large-scale, well-controlled survey of a Norwegian population, found lower than usual concordance figures for monozygotic twins. He gives concordance figures of 25 percent to 38 percent for monozygotic pairs. The personality patterns found in the monozygotic co-twins of his schizophrenic probands are presented in Table 2.

TABLE 2

PERSONALITY PATTERNS IN IDENTICAL TWINS OF PATIENTS

Classification	No.	Percent
Typical schizophrenia	14	31
Reactive psychosis	1	2
Borderline states	3	7
Neurosis	13	29
Normality	14	31
Total co-twins	45	100

In view of the low reliability of psychiatric diagnosis (Ash, 1949), it would appear that another investigator examining the same population might have arrived at different concordance figures. Different diagnostic conventions might well have included reactive psychoses, borderline states, and perhaps some of the more severe neurotic cases with the schizophrenias. It appears likely that the sampling problems previously noted and diagnostic convention account for the lower concordance figures offered by Kringlin.

Rosenthal (1959), confining his investigation to monozygotic twins, found an almost complete absence of schizophrenia in the families of twin pairs which were discordant. This finding is disputed by Kringlin (1966), who found no differences in incidence between the families of concordant and discordant pairs. In concordant twin pairs of the Rosenthal study, 60 percent of the families had a history of schizophrenia.

A recent study by Karlsson (1966), using probands who had been raised in foster homes, avoids many of the criticisms offered by proponents of a social learning theory of the transmission of schizophrenia. Karlsson selected a group of eight probands who had all been placed in foster homes before the age of one year, half of them in the first few weeks of life. The remarkably complete population information maintained in Iceland provided detailed data on the mental health histories of the biologic and foster families of the probands. Twenty-eight of the foster siblings and 29 biologic siblings were obtained for study. Except for two foster siblings who had died, all had reached adulthood, the youngest being 35 years of age. It was found that 6 of the biologic siblings had by that time developed a schizophrenia, but none of the foster siblings showed indication of psychiatric disease.

At the present, genetic studies have succeeded only in showing that schizophrenia is a familial disorder. The basic genetic mechanisms remain to be worked out, and there is notable disagreement among authorities as to the mode of transmission (Fuller & Thompson, 1960). Authorities are fairly evenly split on the question of whether the gene is a dominant or a recessive. Fuller and Thompson (1960, p. 281) sum up the current status of theory in stating "at the present there is no strong evidence for favoring either the simple Mendelian model or the polygenic model." The lack of progress in understanding the genetic transmission of schizophrenia is most clearly attributable to a lack of conceptual clarity about the disorder itself. Genetic studies, following the Munich School, have defined schizophrenia in an "all or none" way and tended to deal with it as though it were a dichotomized trait like the ability to taste phenylthiocarbamide. Operationally, the delineation depends upon hospitalization or psychiatric treatment. This method of proceeding leads to a lack of precision in estimates of the incidence of the disorder. The incidence of a condition must be ascertainable with a fair degree of accuracy in order to apply the statistical tests necessary to determine mode of transmission. The usually accepted incidence figure is around 1 percent. Recent epidemiological studies (Srole, 1962) indicate that this may be a gross underestimate of the true incidence of the disorder in the population. In addition to the previously mentioned sampling problem, major difficulties arise in genetic studies of schizophrenia because the aggregate of behavioral symptoms, which are the basis for this nosological category, cannot be quantified with much precision. Psychiatric diagnosis, which defines the independent variable in these studies, is notoriously unreliable (Sandifer _et al_., 1964). Further, a theory of the etiology of schizophrenia assumes an unnecessary and unrealistic burden if it attempts to encompass all the psychiatric conditions which fall under the rubric "schizophrenia." There is a substantial body of evidence which indicates that schizophrenia is etiologically heterogenous and only phenotypically a unified entity (Bellak, 1958).

Rosenthal's study (1959) of monozygotic twins offers genetic evidence to substantiate the notion of heterogeneity within schizophrenia. He found that in the affected twin of the discordant male pairs, schizophrenia tended to have a later age of onset and a more favorable course than in the concordant male pairs. In the discordant pairs, it was noted that the disease tended to be of the paranoid type, while the catatonic type of reaction was predominant in the concordant pairs. These findings support other genetic studies, such as Kallmann's (1953), which have indicated heterogeneity within schizophrenia and point to a meaningful division between paranoid and nonparanoid forms of the disorder.

In summary, it appears that limitations inherent in psychiatric nosology, and lack of precision in diagnosis, have hampered genetic research in schizophrenia. At the present, concordance rates and empiric risk figures are not sufficiently stable as parameters to permit adequate testing of genetic hypotheses. Consequently, it would appear that a promising research strategy would be to find a group of carefully diagnosed probands who showed a stable biological trait or sign which is characteristic of only schizophrenia among mental illnesses, and to study then the first degree relatives in respect to this trait.

Among genetic theorists, only Kallmann (1953) offers evidence of biological factors which could contribute to the constitutional diathesis. Kallmann's position is that resistance to the manifestation of the mutant gene is regulated by polygenically controlled mesodermal tissue development. Kallmann and Barrera (1942) present evidence to show that the tendency to schizophrenic deterioration corresponds to the presence of a high asthenic (ectomorphic) and a low athletic (mesomorphic) component in body type when classified by Sheldon's method (1940). In that study it was also demonstrated by photographs, spanning from childhood to onset of disease, that in the great majority of identical twin pairs with only one schizophrenic member, the unafflicted twin had always been stronger and taller. Kallmann (1953) subsequently showed that the ability to maintain a stable body weight bore a strong relationship to a favorable prognosis. Kallmann's theory of a polygenic somatic defense offers some explanation of the variable penetrance of the gene for schizophrenia, but does not truly advance genetic conceptions because of the difficulties inherent in the study of polygenic, graded characteristics. Kallmann's data do, however, provide a direct link with the work of Kretschmer and later constitutionalists.

Somatotype

Kretschmer (1925) propounded a theory of a biological affinity between schizophrenia and leptosomatic (asthenic) body build. Kretschmer's description of body types was, to a large extent, based on clinical observations, and only to a limited degree was defined by anthropometric measurements. Sheldon (1940) improved on

Kretschmer's clinical methods and worked from standardized photographs. Sheldon concluded that there were three main components to body build, which he termed ectomorphy, mesomorphy, and endomorphy, because each of these somatotypes appeared to be dominated by structures derived from the three primary embryonic types of tissues: ectoderm, mesoderm, and endoderm. This classification paralleled Kretschmer's asthenic, athletic, and pyknic types. Sheldon's work generally confirmed the affinity between the leptosomatic habitus and schizophrenia.

Rees (1957) summarizes and brings up to date research on physical type in schizophrenia. Rees points out that the bulk of the recent research efforts supports the position that schizophrenics as a group are significantly more leptosomatic than a normal group. However, the consensus which the data from various studies provide supports Kretschmer's theory only in part. They do not confirm his conclusion of a low affinity between schizophrenia and the pyknic type of body build. Although individuals with a pyknic type of body are found sufficiently often in schizophrenic groups to constitute no significant difference from normals, there emerges a persistent negative correlation with the athletic type of body build, or in Sheldon's terms, mesomorphy.

There is evidence to suggest that paranoid schizophrenics tend to be different in body build from the catatonics, hebephrenics, and simple types. Connolly (1939) found that the paranoid schizophrenics tend to be more pyknic in body build than the other types. Rees (1957) cites the works of Mauz, Kisselew, Heberlein, Vanelli, and Langfeldt, which suggest that schizophrenics with ectomorphic body build tend to have an early age of onset and show a greater degree of withdrawal, apathy, and scattered thinking. Schizophrenics of mesomorphic body build, however, tend to have a later age of onset and to show a better preservation of personality and better affective relations.

At the present, evidence provided by the work of the constitutionalists offers support for Kallmann's (1953) contention that manifestation and clinical course in schizophrenia are regulated by a constitutional defense of mesodermal origin. The relationship between mesomorphy and the mesodermal germinal tissue has currently the status of a construct based upon the observation that the mesomorphic habitus reflects primarily the development of the skeletal muscles and structure which are organically involved with their ontogenetic development. Despite the amount of research and the persistence of the negative correlation between development of a schizophrenia and the mesomorphic habitus, no further explanation of the relationship has been offered. The constitutionalists have provided sufficient information to make the degree of mesomorphy attractive as a variation within which to look for a constitutional resistance factor. However, the absence of data indicating an etiological role for the more gross components of mesomorphy, such as the skeletal muscles, dictates that the resistance factor be looked for in mesodermally derived structures which stand in a closer functional relationship to the central nervous system. The cardiovascular system fulfills these requirements. It is of mesodermal origin and is intimately related to the skeletal musculature ontogenetically. It bears known functional relationships to the central nervous system. Although the cardiovascular system shows functional variations in response to mental state, in its morphology it is essentially unchanging. Further, it has been shown by Wertheimer and Wertheimer (1955) that there is a close relationship between mesomorphy and certain morphological characteristics of the vascular system. Wertheimer and Wertheimer report a significant negative relationship between amount of subpapillary plexus and degree of mesomorphy. The mesomorphy ratings in this study were made by Dr. William Sheldon.

Cardiovascular System

The cardiovascular system, which is of mesodermal origin itself and is intimately involved with the development of other mesodermal structures, has been found to show marked differences from normal in schizophrenic populations. N. D. C. Lewis (1923) reported that a hypoplastic circulatory apparatus was consistently found at autopsy in catatonics and hebephrenics. He stated that the heart was approximately one-third smaller in these types of schizophrenics than in normals. He also reported that he had found small visceral capillaries in cases with small hearts. Heart size alone significantly differentiated catatonic and hebephrenic patients from paranoid schizophrenics. David (1957) reviews the literature and finds that Lewis's work has been generally confirmed by a majority of investigators. This finding is of particular interest in view of reports that paranoid schizophrenics tend to differ from other types of schizophrenia in body build, having a greater tendency to the pyknic build (Rees, 1957).

Shattock (1950) carried out an extensive and carefully controlled clinical study on the somatic manifestations in schizophrenia, with particular attention to the phenomena of cyanosis. She found that the schizophrenic patients could be clearly differentiated from affective psychotics and normal controls on the basis of manifest impairment in the peripheral circulation. It was further found by observation of retinal vessels of schizophrenics that there was a wider field of vessel constriction. However, it was noted that circulatory differences were not apparent in studies of total cerebral blood flow. Kety (1948), using the nitrous oxide technique, was not able to show differences in cerebral blood flow and oxygen consumption. As Richter (1957) points out, Kety's work does not exclude an impairment of local circulation, especially under more basal conditions. Serota (1939) has shown the complexity of local circulatory mechanisms normally operating in the brain, and feels that it may be significant that the most highly vascular region of the brain is the hypothalmus. Filipini (1947) found consistent capillary abnormalities in the brains of a carefully diagnosed series of schizophrenic patients who were brought to autopsy. David (1957) reported that the _Schwundzell_ (dwarf cell) alteration found by Vogt and Vogt strongly suggests mild cellular anoxia. Davidson (1956) concludes that the constitutional somatic manifestations of the disease should be sought within the capillary endothelium of the brain. Support of this idea can be found in the dramatic, though transitory, improvement of stuporous catatonics after inhalation of CO_2. Wolff and Lennox (1930) suggest that this improvement is attributable to transitory capillary dilation and increased blood flow. Cobb and Fremont-Smith (1931) were able to confirm this effect of CO_2, and they observed the increased blood flow in the retina.

Richter (1957) in his review of the biochemical aspects of schizophrenia concludes that there is evidence of a defect in the homeostatic mechanisms which may be directly attributed to a defect in circulatory control. Maricq (1963a), too, points out that the biochemical substances thought to be involved in the pathogenesis of schizophrenia, such as seratonin, catecholamines, histamine, and bradykinin, are the same vaso-active mediators known to participate in the regulation of the microcirculation.

Capillaries of the Nailfold

The relationship of the nailfold capillary network to the vessels lying beneath the surface of the skin was intensively studied by Spalteholz (1927) and Sir Thomas Lewis (1927). Jaensch (1929) showed that there were relationships between anomalies in capillary morphology and a variety of physical and psychiatric disorders. These efforts produced a number of schemes for the classification of the different shapes which the skin capillaries assume. Lovett-Doust (1955) has refined classification of the skin capillaries and found nine morphological types which can be identified reliably. Wertheimer and Wertheimer (1955) demonstrated that, within the different morphological categories, the parameters of length, thickness, twisting, and degree of subpapillary plexus could be quantified with high reliability.

A schematic cross section of the skin is shown in Figure 1. The two major layers, the corium and epidermis, originate from mesodermal and ectodermal tissue respectively. The subpapillary plexus consists of the network of vessels composed of both arterial vessels sending blood into the capillaries and venous vessels which collect the blood returning from the capillaries. The plexus lies at the base of the corium and is horizontal to the skin surface. The end row loops extend vertically from the subpapillary plexus into the corpus capillare. In the normal mature condition, they assume the shape of small hairpins. In the infant, no end row loops are present, and only the subpapillary plexus can be seen. By five months of age the

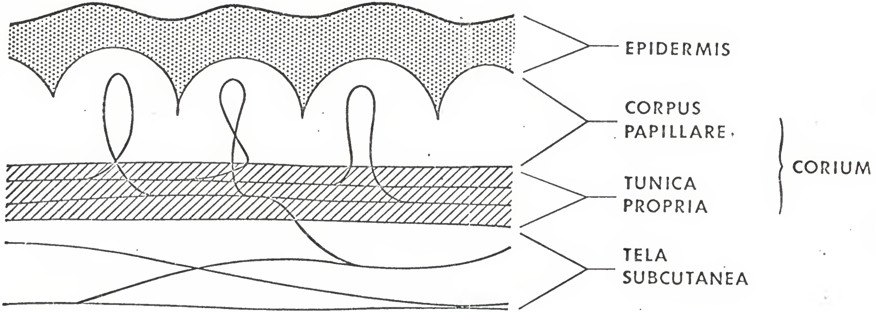

Figure 1.--Schematic cross section of the skin.

plexus begins to recede and there is some end row loop formation (Hauptmann & Meyerson, 1948). The precise age in a given child at which the plexus disappears varies considerably, but by puberty the plexus has receded in almost all cases. Hauptmann and Meyerson (1948) state that a subpapillary plexus is never found in the normal adult. Maricq (1965) conducted a survey of capillary maturation in normal children, and reports that a plexus is found in only 3 percent of this group after the age of 15 years. Once the capillaries assume the adult form there is little if any change. Previous works have stated that there was no change at all. Hauptmann and Meyerson (1948, p. 92) maintain that "the capillaries are as characteristic of a given person as his face, and that they remain the same from day to day and from minute to minute." A report by Maricq (1966) indicates that a change in plexus has been observed in a few cases. This finding remains unconfirmed. The bulk of the evidence supports the view that the capillary morphology remains constant and is not changed by such factors as aging, environment, or course of psychiatric illness (Norris & Chowning, 1964).

Anomalies in the nailfold capillary patterns have long been noted in mentally ill patients. Research in this area over a period of 40 years has shown an encouraging consistency in the results obtained by various investigators. Reviews of this literature have been presented by Hauptmann and Meyerson (1948), Wertheimer and Wertheimer (1955), and Lovett-Doust (1950). In general, it has been found that a visible subpapillary plexus appears more frequently in schizophrenics than in normals, and never appears in any other diagnostic category, with the exception of some forms of endogenous mental retardation (Maricq, 1965). Not only can the schizophrenic be distinguished from the normal, but also the paranoid subtype can be further differentiated from the rest of the schizophrenic reactions (Wertheimer & Wertheimer, 1955; Lovett-Doust, 1955). Hauptmann and Meyerson (1948) reported that 71.5 percent of their schizophrenic subjects had a visible subpapillary plexus. The remaining 28.5 percent who did not show a prominent plexus included both those patients with more marked paranoid symptoms, and patients for whom the original diagnosis was unclear. Maricq (1963a, 1963b) found that there were major differences in the amount of plexus between schizophrenic patients who had a positive family history for the disorder, and patients who did not have a positive family history. Norris and Chowning (1964) and Maricq (1963a) have noted that a high degree of visible plexus is positively related to poor prognosis. Twin studies by Schiller (1937), Lehmann and Hartlieb (1938), and Osato and Awano (1957) are all in agreement that the form of the capillary patterns are largely determined by heredity.

Summary

The more comprehensive of both monogenic-biochemical and diathesis-stress theories, as presented by Kallmann (1953) and Meehl (1962) respectively, posit a constitutional defense against the manifestation of a schizophrenic psychosis. The use of the term "constitutional defense," at this stage of theory development, lacks precision: The way in which the constitutional factors defend against the development of a schizophrenic reaction is not known. At the present, the search for a constitutional factor in the specific etiology requires no more than looking for a biological component which is a distinguishing characteristic for schizophrenia and which is inversely related to the severity of the disorder.

The search for biological differences in schizophrenia has been disappointing. In addition to the difficulties imposed by the effects of psychosis itself, and hospitalization and treatment, the concept that schizophrenia is a unitary process or a disease entity has most likely hampered research. As was noted in previous sections, the data from a number of different approaches indicate heterogeneity and a division between paranoid and other than paranoid forms. Lack of homogeneity in the category "schizophrenia" as an independent variable would obscure true differences in the usual comparisons with other groups such as normals, organics, and neurotics. The result would be that differences which are valid for some kinds of schizophrenia would frequently be obscured by sample composition, but would finally appear as persistent differences of a low order of magnitude. In the large body of research on the etiology of schizophrenia, a number of such low-order, persistent differences have emerged which are themselves interrelated.

A low mesomorphic component in somatype is characteristic of those schizophrenics which have the earliest age of onset, poorest prognosis, greatest degree of affective and thought disturbances, and highest incidence of the disorder in genetic studies of their families. This same group has also shown the greatest divergence from normal on all biological parameters, and more specifically in cardiovascular anomalies. Studies of the capillaries of schizophrenics show that those with the most subpapillary plexus are described in exactly the same terms, and that in addition there is a strong negative relationship between the amount of mesomorphy and the degree of visible plexus. Therefore, it appears likely that the conditions which permit the plexus to be visible contribute to the constitutional diathesis in schizophrenia. Further, Hauptmann and Meyerson (1948) from their extensive studies conclude that the amount of plexus increases as a function of the similarity with which the schizophrenic manifestations of the patient resemble classical dementia praecox, which since Bleuler (1911) has been widely held to be etiologically dependent upon constitutional factors.

Meehl's (1962) theory offers an advantage in conceptualizing schizophrenia as an uncompensated or decompensated subset within the more inclusive class schizotypy. Meehl holds that the essential characteristics differ only quantitatively between mild schizotypy and overt schizophrenia. In diathesis-stress terms, the constitutional capacity to respond to stress with a schizophrenic reaction would exist prior to the development of the disorder. In Meehl's conception, the pre-schizophrenic person exhibits characteristic schizotypic behavior and possesses the genetic constitutional vulnerability while still in a subclinical status. Thus it should be possible to delineate more clearly the relationships between the psychological and biological components of the disorder before the onset of overt psychosis. Discrimination is desirable at this early stage because the psychotic process itself disrupts the psychobiological organization of the person, thereby obscuring the relationship between these two components. In terms of Meehl's theory, the degree of schizotypy is expected to be related positively to the amount of deficit in those biological factors which make up the constitutional defense. From the studies cited above, it appears that those biological factors which permit the plexus to be visible play a prominent role in the constitutional defense against the development of a schizophrenic reaction. Following this line of speculation, the central purpose of this research is to establish that the plexus is genetically controlled, and that there is a positive relationship between the amount of plexus and the degree of schizotypy.

Hypotheses

1. Schizophrenic subjects who have a family history positive for a major mental illness will show a greater amount of subpapillary plexus than schizophrenic subjects with a family history negative for mental illness.

2. In schizophrenic subjects, the degree of subpapillary plexus is inversely related to good prognosis.

3. In family comparisons spanning at least two generations, it can be demonstrated that a visible plexus is a heritable characteristic.

4. In first-degree relatives of schizophrenic probands, there is a positive correlation between amount of subpapillary plexus and degree of schizotypy.

CHAPTER II

EXPERIMENTAL PROCEDURE

Study I: In-Hospital Study

Subjects and Procedures

The subject pool for the family history comparisons consisted of all patients carrying a diagnosis of schizophrenia who were on the roster of the Northeast Florida State Hospital on the target date, January 1, 1965, and who met the criteria of being between the ages of 14 and 60, white, and without diagnosed organic disease. Because of the unreliability of hospital diagnosis, the following additional criteria were imposed to insure the diagnostic homogeneity of the subject (S) pool: All subjects (Ss) had to have a history of hallucinations, delusions, or other markedly bizarre behavior. This assured a clear-cut and uncomplicated diagnosis of schizophrenia. There were 233 patients who met these criteria. Additional patients who met the criteria were added from consecutive admissions, raising the total number to 246. Of this group, 60 patients were reported (in a routine social service questionnaire) to have a positive family history of a major psychiatric disease. Patients were considered to have a positive family history when they had a blood relative who had either been hospitalized for psychosis or had been under the care of a physician for a severe psychiatric disturbance. Negative family histories were those in which the questionnaire respondents denied the presence of psychiatric disease in the family. The number of families reporting negative histories was 57. There was no history for 47 patients, whose families failed to respond. Of the original subject pool of 246, 82 of the patients were out of the hospital on leave and were not available for study, leaving a total sample of 164 Ss.

The 50 male Ss used for comparison on the Phillips Prognostic Rating Scale (PRS) were selected from the original subject pool. They were all between the ages of 18 and 45. The age range was restricted for this sample because the item content of the PRS is most appropriate for male post-adolescents. The sample was further restricted in order to get proportional numbers from both the chronic and acute wards of the hospital. These two subgroups were combined to insure that the sample would be representative in terms of chronicity.

The Prognostic Rating Scale

The Prognostic Rating Scale (Appendix A) was developed and validated by Phillips (1953). The pre-morbid history subscale was selected for use in this portion of the study because of its demonstrated ability to predict good and poor prognosis (Phillips, 1953).

The pre-morbid history subscale includes 20 items: 7 items on the social aspect of sexual life during adolescence and immediately beyond; 7 items on recent sexual life; and 6 items on recent pre-morbid adjustment in personal relations. Each subsection of item type yields an independent score. The over-all score is obtained by summing all the subsection scores. All scores are derived by counting the number of items checked. The subsections of the scale which reflect sexual adjustment have proven to be the most successful in predicting the outcome of treatment (Phillips, 1953).

Plexus Evaluation

Visualization of the capillaries is best accomplished in the skin of the nailfold. In other skin areas, only the top bend of the capillary loop would be visible. Figure 2 is a schematic cross section of the skin as it

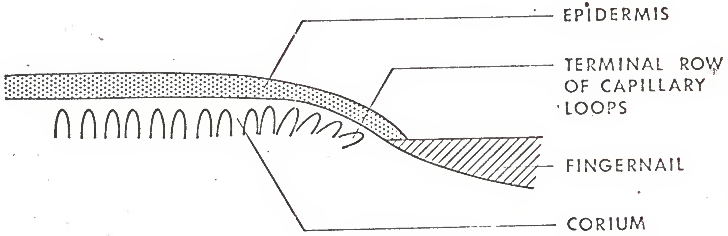

Figure 2.--Schematic cross section of the skin as it forms the nailfold.

forms the nailfold. From this perspective, the end row loops can be easily visualized, since the tapering off of the dermal and ectodermal tissue layers into the nailfold forces the capillary loops into a more or less horizontal position. The observational field includes the entire nailfold crescent and extends proximally between one and two millimeters.

For observation of the capillaries, a Wild M5 microscope was employed. Using the 10x pair of wide-field eyepieces, over-all magnifications were obtained of 6x, 12x, 25x, and 50x. The 12x magnification proved the best compromise between breadth of field and clarity of detail in the capillary network. The light source was two Wild low-voltage lamps fitted with six-volt 15-watt incandescent bulbs and supplied by a regulating transformer from a 110/220 vac line. The lamps were fitted with green filters to provide increased contrast of the capillaries.

The fourth and fifth fingers on the subject's hands were used for rating purposes, following the recommendations of Hauptmann and Meyerson (1948). The fingers were first washed with 90 percent alcohol and then treated with a small drop of immersion oil. The immersion oil reduces light reflection from the scaly outer layers of the epidermis and facilitates visualization of the small blood vessels. The subjects' fingers were held by the Examiner (E), in such a way that they could be moved freely on the microscope stage. This procedure was found to be preferable to maintaining a fixed position, because for an accurate plexus rating the entire nailfold crescent must be searched and the natural undulations in the tissue layers require continuous refocusing of the microscope.

Figure 3 is a schematic drawing showing the different grades of plexus. Zero (0) indicates the absence of any visible plexus. Grade 1 describes a plexus consisting of only a few short branches. In a Grade 1 plexus, two to four loops are joined at the base by horizontal branches. A Grade 2 plexus consists of a number of loops joined at the base by horizontal vessels. The Grade 2 plexus does not exceed more than two rows of loops in a proximal direction. The Grade 2 condition is often localized in area and may be found in one side of the nailfold crescent. Grade 3 refers to a clearly developed plexus which begins at the base of the end rows and extends for some distance proximally. The Grade 3 condition is characterized by a visible plexus around the entire nailfold crescent. Grade 4 is the most extreme degree of plexus and extends a considerable distance proximally.

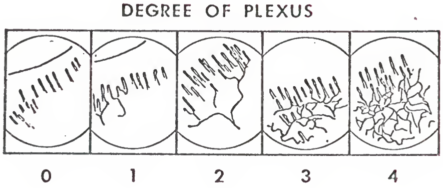

Figure 3.--Schematic drawing of the different grades of subpapillary plexus.

In order to insure reliability of plexus ratings, one week was spent examining a psychiatric population under the supervision of Dr. Hildegard Maricq, who has conducted extensive research on the nailfold capillaries.

A nurse, who was experienced in microscopic techniques, was then trained in capillary evaluation. An initial group of 36 normal subjects was examined by both raters for purposes of familiarization with the normal capillary picture. An additional group of 100 patients with a hospital diagnosis of schizophrenia was then examined independently by both raters. During these examinations, comparisons were continuously made with photographs of the different degrees of plexus which were obtained by Wertheimer and Wertheimer (1955). Ratings were compared between the two examiners for the patients utilized in the pilot study. These ratings were made in terms of half-scale units, and yielded an $\underline{r} \doteq .92$.

Method

To test Hypothesis 1, that a relationship exists between degree of visible subpapillary plexus and a family history positive for mental illness, the 164 Ss were examined for plexus and for family history. The plexus ratings were made following the procedure described above. Both raters examined each patient and averaged the eight observations made on the four fingers to give a final plexus rating. The family history data were obtained from questionnaires completed by the family of the patient at the time of the patient's admission. The questionnaire contained three questions pertinent to the present study: (1) Was any member of your family ever hospitalized for a nervous or mental illness?; (2) Was any member of your family ever in out-patient treatment for a nervous or mental illness?; (3) Describe briefly the nature of the nervous or mental illness. If responses to these questions were affirmative, the family history was classified as positive. If the responses were negative, the family history was classified as negative.

Hypothesis 2, the relationship between plexus and prognosis, was approached by administering the PRS individually to the 50 patients who met the previously determined criteria for this phase of Study I. The _E_ administering the PRS had no knowledge of the plexus ratings which had been obtained on each _S_ as previously described. The extent of plexus was then compared with the magnitude of prognostic ratings. It was predicted that the greater the degree of plexus, the higher the score on the PRS.

Study II: Within-Family Study

Subjects and Procedures

Subjects.--Subjects were chosen by selecting probands who exhibited both schizophrenia and the somatic sign, a visible subpapillary plexus, as well as meeting other criteria and practical considerations detailed below. Appendix B presents the age, sex, diagnosis, age of onset, number of siblings, family history (separately for the maternal and paternal sides), number of hospitalizations and their total length, for each of the probands. The selection process was as follows:

1. Hospital records were surveyed to establish a pool of patients diagnosed as schizophrenic.

2. Plexus ratings were obtained for all these patients, and those with a high rating were placed in the pool of Ss who had met the critical double criterion.

3. From this pool, 50 probands who, on the basis of hospital records, had an intact and reachable family were chosen.

4. Sixteen of these potential Ss were deleted from the study either because the families were, in fact, unavailable, or because it was not possible to obtain the

minimum five hours necessary to complete reliable schizotypy ratings on each member of the family.

The families of these 34 probands were the _S_s utilized in the comparisons of Study II. No proband had less than 2 available first-degree relatives. The total number of first-degree relatives was 106.

Schizotypy ratings.--The schizotypy ratings were made on the basis of a check list of schizotypic signs constructed by Meehl (1964). This check list, with the weights for the various items, is found in Appendix D. A detailed manual to assist the clinician in these schizotypic signs has been compiled by Meehl (1964). The purpose of the check list is to objectify and quantify the clinical assessment of schizoid tendency or schizotypic signs. The observational data required to arrive at the listed judgments are gathered chiefly from diagnostic interview. Additional information from informants, documents, and psychometric study may be used as supplementary data, if available. Each item on the scale is scored as either present or absent. The final score on the Schizotypy Rating Scale is a summation of the weighted items. The instructions explicitly state that the clinician should check the symptom or trait only if he is highly confident of its presence. If the rater finds himself wondering whether or not a sign should be checked, the symptom is not clearly in evidence and should not be checked. Meehl (1964) recommends a minimum of at least five hours' contact with the person before an accurate rating can be made. Meehl's recommendations were closely followed in making the schizotypy ratings.

Plexus evaluation.--The microscope and microscopic procedure used in examining the plexus as well as a description of the grades of plexus has been described in detail on pages 33-38.

Method

Subpapillary plexus and schizotypy ratings were obtained on all available first-degree relatives of the 34 probands. Plexus ratings were made by the assistant E in order to assure independence between the plexus ratings and the ratings on the Schizotypy Rating Scale made by the E. To insure E's constancy of judgment in the Within-Family Study, both raters examined, at monthly intervals, patients who were not included in the study. Agreement between the two raters remained highly consistent.

In addition to interviewing each subject to complete the Schizotypy Rating Scale, all other available sources of information about the *S*s were utilized. In the interviews with each member of the family, information was obtained about all other members of the family. Letters from members of the family to the patients who were probands in this study, and correspondence between the families and the hospital, were examined. Information about various family members was obtained from the social workers and physicians who had had contact with them. A provisional check list was made out for each *S*'s contact until the *E* was confident that he had obtained an accurate picture of the subject. The numbers of hours of contact with *S*s varied from the minimum of 5 to a maximum of 12. The method of continuous revision of the check list and utilizing information about the subject from other members of the family proved valuable. For example, through one or two interviews the subject might offer no information which would make it possible to evaluate a given item, despite the fact that other family members characterized the subject as having this trait. In such circumstances, direct questioning on this particular item in later interviews elicited information which made it possible to assess the item in question.

Hypothesis 3, the heritability of a visible subpapillary plexus, was explored by comparing the plexus ratings of the parents and their offspring in the families of the probands. The probands, of course, were excluded from these comparisons.

Hypothesis 4, the relationship between plexus and schizotypy, was studied by comparing the obtained subpapillary plexus ratings with the schizotypy ratings for each of the 106 _S_s in the probands' families.

CHAPTER III

RESULTS

Study I: In-Hospital Study

Hypothesis 1 was tested by means of a two-tailed _t_ test for independent means. The comparisons between mean plexus ratings for each family history classification (that is, positive, negative, and no information) failed to substantiate the hypothesis that schizophrenic _S_s with a family history positive for mental illness will show a greater amount of subpapillary plexus. For this sample, then,mean plexus ratings show no significant variation as a function of family history for mental illness.

Since additional data were available for the _S_s, the possibility existed of finding relationships among variables other than those included in the stated hypotheses. Means and standard deviations for the plexus rating, age, age of onset, duration of illness, and number and length of hospitalizations as a function of family history are presented in Table 3. Age, age of onset, and duration of illness are related variables: Duration of illness equals age minus age of onset.

TABLE 3

MEANS AND STANDARD DEVIATIONS FOR THE PLEXUS RATING, AGE, AGE OF ONSET, DURATION OF ILLNESS, NUMBER AND LENGTH OF HOSPITALIZATIONS AS A FUNCTION OF FAMILY HISTORY (POSITIVE, NEGATIVE, OR NO INFORMATION)

Variable	Positive (N=60)		Negative (N=57)		No Information (N=47)	
	X	sd	X	sd	X	sd
Plexus rating	2.1	1.1	2.1	1.4	2.1	1.2
Age	35.8	14.3	38.1	12.9	36.1	13.0
Age of onset	28.0	12.7	30.5	10.2	34.0	12.6
Duration of illness (years)	7.7	8.5	7.6	7.7	2.1	2.6
Number of hospitalizations	3.2	2.1	2.5	1.2	1.7	0.9
Length of hospitalization (months)	37.7	55.2	39.2	47.5	15.4	16.3

In summary, the results of these analyses show that the principal differences regarding family history involve patients whose families failed to respond to the questionnaire. This group has been ill for a shorter period of time, and has been hospitalized fewer times and for a shorter total period of time than either of the other two groups. The only significant difference between the positive and negative groups was the difference in number of hospitalizations.

All of these differences were significant at the .05 level of confidence.

Various relationships to plexus ratings are presented in Table 4. Correlations between plexus rating and age, age on onset, duration of illness, and number and length of hospitalizations are shown. Both total and within-group correlations are presented. In the total correlations, deviations were taken from the mean of all 164 patients, while in the within-group correlations deviations were taken from the mean of all patients of the same sex and family history, positive, negative, or no informa-

TABLE 4

WITHIN-GROUP CORRELATIONS BETWEEN THE PLEXUS RATING AND AGE, AGE OF ONSET, DURATION OF ILLNESS, NUMBER AND LENGTH OF HOSPITALIZATIONS

Variable	Correlation with Plexus	
	Total	Within-Group
Age	.06	.05
Age of onset	.01	-.00
Duration of illness (years)	.08	.07
Number of hospitalizations	-.08	-.06
Length of hospitalizations (months)	.12	.09

tion. The correlations are all negligible and nonsignificant.

Means and standard deviations for plexus rating, age, age of onset, duration of illness, and number and length of hospitalization as a function of gender are summarized in Table 5. The females are older and have a later age of onset than the males; significance reaches the .05 level in both cases. None of the other differences is significant.

TABLE 5

MEANS AND STANDARD DEVIATIONS FOR THE PLEXUS RATING, AGE, AGE OF ONSET, DURATION OF ILLNESS, NUMBER AND LENGTH OF HOSPITALIZATIONS IN MALE AND FEMALE POPULATION

Variables	Male (N=60)		Female (N=104)	
	X	sd	X	sd
Plexus rating	2.0	1.2	2.1	1.2
Age	33.9	12.4	38.3	13.8
Age of onset	28.2	10.6	32.0	12.7
Duration of illness (years)	5.6	7.9	6.3	7.2
Number of hospitalizations	2.4	1.4	2.6	1.7
Length of hospitalizations (months)	24.3	40.7	36.2	47.8

In addition to these data, since differential diagnostic classifications were available for the schizophrenic Ss showing plexus, t tests were computed between the mean plexus ratings for paranoid, chronic undifferentiated, and "other" diagnostic classifications.

Plexus rating as a function of diagnosis is shown in Table 6. The mean difference between the paranoid and the other two groups of patients reaches significance at the .05 level.

TABLE 6

SUBPAPILLARY PLEXUS RATING AS A FUNCTION OF DIAGNOSIS

Diagnosis	N	X	sd
Paranoid	45	1.90	1.2
Chronic undifferentiated	81	2.06	1.2
Other schizophrenias	38[a]	2.41	1.1

[a] Includes catatonic (11), hebephrenic (7), acute undifferentiated (8), schizo-affective (10), and simple (2).

Hypothesis 2 was tested by computing a Pearson product-moment coefficient of correlation between degree of plexus and scores on the PRS. The analysis yielded a correlation coefficient of .65, which is significant at the .01 level of confidence. These findings support the hypothesis that the degree of subpapillary plexus is inversely related to good prognosis.

Study II: Within-Family Study

Hypothesis 3, "In family comparisons spanning at least two generations, it can be demonstrated that a visible plexus is a heritable characteristic," was strongly supported by the finding of almost identical average plexus ratings between the two generations.

In order to make a valid comparison between the two generations, children should be compared only with their parents. There were 19 families for which data were available for both parents, and for at least one sibling of the proband. To compare the two generations, the average sibling rating in each family (the mid-sibling) was obtained. If there was only one sibling, then this rating was the mid-sibling. If there were three siblings other than the proband, then the mid-sibling was the average of the three ratings. In this manner, 19 mid-parental and 19 corresponding mid-sibling ratings were derived, and the two sets of ratings were paired, parents with their own children.

For the plexus ratings, the mid-parental average was 1.79, and the mid-sibling average was 1.80. There was no appreciable drop from parent to child, which speaks strongly for the heritability of the plexus.

In 10 of the 19 families there was at least one brother and in 14 families there was at least one sister to the proband. Mid-brother and mid-sister ratings were compared in the same way as the mid-sibling ratings. When the mid-measures were averaged, means were obtained of 1.39 for the mid-brothers and 2.11 for the mid-sisters. Using these mid-measures, it was possible to develop a more sophisticated test of significance. The mid-brother rating in Family X differed from its mid-parent by a definite amount; similarly, the mid-sister rating in Family Y deviated by a determinant amount from its mid-parent. In total, there were 10 mid-parent minus mid-brother differences and 14 mid-parent minus mid-sister differences. These differences in plexus were treated as uncorrelated arrays. A t value of 2.26 was obtained, which is significant at the .05 level. It can be concluded that, while the average mid-sibling's rating is identical with the average of corresponding mid-parents, the average mid-brother's rating is significantly smaller than the average mid-sister's rating, when both mid-measures are taken in relation to their corresponding mid-parent. It would seem, therefore, that there is differential penetrance for plexus in males and females; in this rather special population a common genotype appears more strongly in the female.

Marital correlations between the parents of 32 probands were examined. In these 32 cases where both parents were available, it was possible to calculate the correlation between fathers' and mothers' ratings for both plexus and schizotypy. The results were unexpected. The Pearson product-moment correlation between fathers' and mothers' plexus ratings was -.48, which is significant at the .01 level; the marital correlation for the schizotypy ratings, again a Pearson coefficient, is -.35, which is significant at the .05 level. In Figure 4, a scatter diagram for the schizotypy ratings is presented. The negative relationship is apparent. These correlations mean that families in which both parents have either high or low plexus (or schizotypy) ratings are underrepresented in the present sample. If one parent has a low rating, the other tends to have a high one, and vice versa.

The test of Hypothesis 4, the main comparison of the study, takes the form of a partial rank correlation coefficient within families between schizotypy and plexus ratings. In each family the relatives (excluding the proband) are ranked according to the size of their plexus rating. The partial rank correlation is based upon the extent to which the schizotypy ratings in each family fall

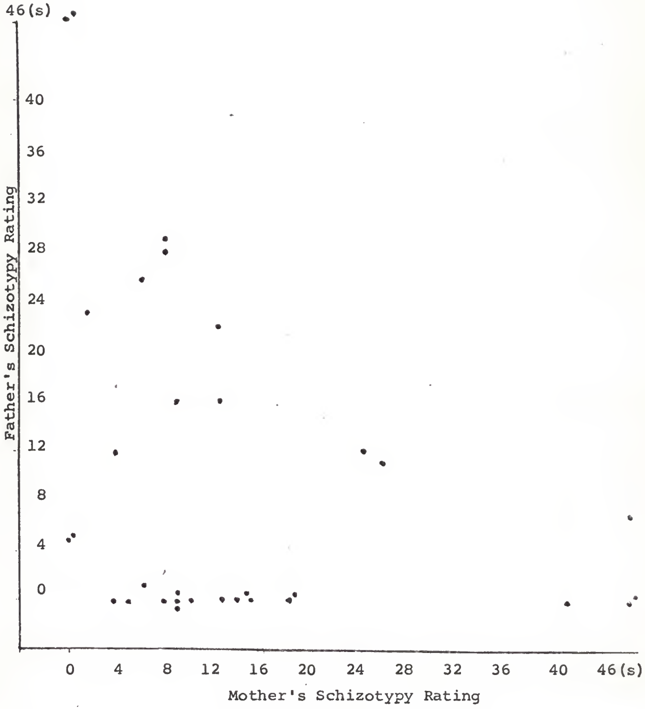

Figure 4.--Scatter diagram for schizotypy ratings of the probands' mothers and fathers.

into the same alignment as the plexus ratings. The counts on which the coefficient is based are made within each family, so that the differences from one family to the next are ignored.

The partial rank correlation between schizotypy and plexus equals .56. This value is significant well beyond the .001 level. In a normal population a rank correlation of .56 corresponds to a Pearson product-moment coefficient of .77. At this point it may be well to underscore again that the plexus and schizotypy ratings were made by two different investigators, each of whom was blind to the other's results.

Kendall's partial rank correlations (Siegel, 1956) were run between age and plexus rating, and age and schizotypy ratings. The results were .07 and .09 respectively. These values are much too small to indicate either statistical significance or any appreciable role for age in mediating the relationship between plexus and schizotypy ratings.

Table 7 contains means and standard deviations based on the data in Appendix B. Means and standard deviations are presented for the probands, their parents,and siblings, on the variables of sex, age, schizotypy, and plexus ratings. In making these calculations, a relative who was or had been hospitalized for schizophrenia was given an arbitrary

TABLE 7

MEANS AND STANDARD DEVIATIONS FOR AGE, PLEXUS RATINGS, AND SCHIZOTYPY RATINGS AMONG THE 34 PROBANDS, THEIR PARENTS, AND THEIR SIBLINGS

Subjects		Age		Plexus Rating		Schizotypy Rating	
	N	X	sd	X	sd	X	sd
Probands Female	18	21.1	4.9	3.3	0.9	46.0	0.0
Probands Male	16	22.4	4.6	3.2	0.6	46.0	0.0
Probands	34	21.7	4.8	3.3	0.8	46.0	0.0
Fathers	32	50.8	6.4	1.3	1.5	9.5	13.3
Mothers	34	48.8	5.8	2.1	0.9	14.3	13.2
Parents	66	49.8	6.2	1.7	1.3	12.0	13.4
Brothers	13	21.2	4.1	1.5	0.9	9.3	8.1
Sisters	27	21.1	4.4	2.2	1.1	8.7	7.9
Siblings	40	21.2	4.3	2.0	1.1	8.9	8.0

schizotypy rating of 46, the maximum.

The principal feature of the data in Table 7 is the tendency for mothers and sisters to have higher plexus ratings than fathers and brothers. The mean plexus rating for mothers (2.1) is significantly larger than the mean plexus rating for fathers (1.3) at the .05 level by a two-tail *t* test for correlated means. The test excluded the two probands whose fathers could not be located. The mothers have a higher mean schizotypy rating than the fathers, but significance does not reach the .05 level. The sisters' average plexus rating (2.2) was larger than the brothers' average rating (1.5). However, the difference was not statistically significant ($\underline{p} > .05$). In this case a $\underline{t}$ test for uncorrelated means was used because only 5 of the 34 families contained siblings (other than the proband) of both genders. The schizotypy ratings of brothers and sisters were substantially the same.

The finding that mothers have a significantly higher plexus rating than fathers requires further examination of the data in terms of parental predominance. The trend toward parental predominance favoring the mother also needs further examination, in view of the high correlation between schizotypy and plexus.

Parental predominance means that one of the two parents has the higher rating for schizotypy or plexus, whichever the case may be. In the present data, shown in Table 8, the two kinds of predominance are closely associated. In the analyses, one pair of parents had the same plexus rating; hence neither parent was predominant and the family was excluded. The results of the chi-square analyses were quite

TABLE 8

PARENTAL CONCORDANCE OF SCHIZOTYPY AND PLEXUS

Schizotypy	Plexus		Total
	Mother	Father	
Mother	19	0	19
Father	3	9	12
TOTAL	22	9	31

Note: $p < .001$ by Fisher's exact test.

clear. If the father is predominant on the plexus rating, he tends to be predominant on the schizotypy rating also, and vice versa. The result is significant beyond the .001 level by Fisher's exact test.

The proband's sex is not related to parental dominance. On a chi-square analysis, the two sexes divide evenly for both plexus and schizotypy ratings regardless of parental predominance.

When the parents were interviewed for the schizotypy ratings, they were also asked about mental illness in their families. Each parent was asked both about his own and his spouse's families. These data appear in Appendix B. On the basis of these data, each family was placed into one of four categories: those which had a positive history on the mother's side, on the father's side only, on both sides, and on neither side.

Parental predominance on the schizotypy ratings as a function of family history is presented in Table 9. The

TABLE 9

PARENTAL PREDOMINANCE ON THE SCHIZOTYPY RATING AS A FUNCTION OF POSITIVE FAMILY HISTORY

Schizotypy Predominance	Positive Family History				
	Father Only	Mother Only	Both	Neither	Total
Mother	0	6	3	11	20
Father	5	2	2	3	12
TOTAL	5	8	5	14	32

	Consolidating		
	Father Only	Other Groups	Total
Mother	0	20	20
Father	5	7	12
TOTAL	5	27	32

Note: $p < .01$ by Fisher's exact test.

most noteworthy feature of the analysis is that, when the family history is positive on the father's side only, parental predominance always favors the father. When Table 9 was collapsed by pooling the mother's side only, both sides, and neither side into one category, the resulting analysis was significant at the .01 level by Fisher's exact test.

Parental predominance on the plexus rating as a function of family history is presented in Table 10. Again, there is a tendency for predominance of plexus to be on the father's side in couples which have a positive history only on the father's side. This time, however, the result was not significant. Even when the data were pooled for the three categories other than fathers only, Fisher's test failed to show significance.

A serendipitous finding, not relevant either to the initial hypothesis or to the previous analyses, needs to be described. During the course of the hospital population study, an unusual condition in the nailfold was observed which will have important consequences in the classification of the capillaries. In Figure 2, it can be seen that there is a gradual tapering of the skin into the cuticle, which forces the end row loops into a horizontal position. In the normal condition, at least one row of end loops is

TABLE 10

PARENTAL PREDOMINANCE ON THE PLEXUS RATING AS A FUNCTION OF POSITIVE FAMILY HISTORY

Plexus Predominance	Positive Family History: Father Only	Mother Only	Both	Neither	Total
Mother	2	6	3	11	22
Father	3	2	2	2	9
TOTAL	5[a]	8[a]	5	13	31

	Consolidating: Father Only	Other Groups	Total
Mother	2	20	22
Father	3	6	9
TOTAL	5	26	31

[a] One couple with tied plexus rating.

Note: p does not reach the .05 level.

always seen. In the typical picture of the schizophrenic, several rows of loops are seen, even when there is only a small amount of plexus. In the condition schematically described in Figure 5, which we shall call "folding," no end row loops at all are visible. In this "folding" condition,

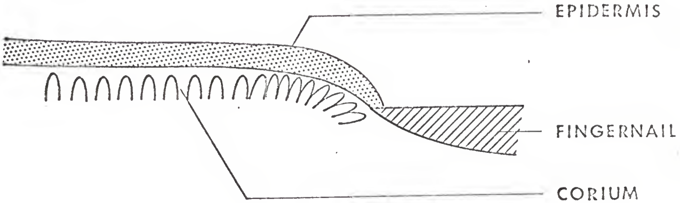

Figure 5.--Schematic drawing of the folding condition.

the terminus of the corium is quite thick, rather than tapering off. It is often scalloped in the vertical dimension, and the tops of the bend in the capillary loops can be seen in several layers.

This condition almost always extends the entire perimeter of the nailfold crescent. There are, however, exceptions, two of which initially called attention to this condition. In the first patient in whom this condition was noted, the folding occurred only in the center of the nailfold crescents with no end row loops visible in this portion. On both sides of the fold there was a clear Grade 3 plexus with long, slender, end row loops. Figure 6 illustrates this example. The second sample showed folding around the crescent except for an area the shape of a small bight which opened at the center line of the nailfold crescent. Figure 7 illustrates this condition.

In examining subsequent patients who showed "folding," it was found that in some cases the fold could be manually pulled back, exposing the underlying end row loops connected by the horizontal vessels which form the plexus. This indicated that plexus was present, but no further evaluation could be made. However, it was found that the folding condition is a graded characteristic, and

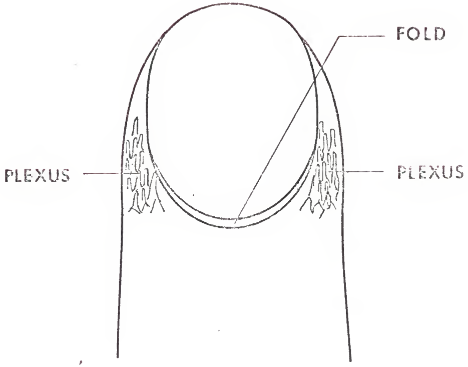

Figure 6.--Folding condition 1.

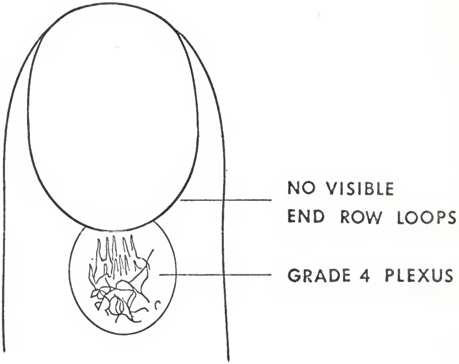

Figure 7.--Folding condition 2.

that in some cases a moderate degree of folding could be observed which only partially obscured the plexus. For the 106 subjects in the within-family phase of the study, folding occurred in 12 percent to some degree.

CHAPTER IV

DISCUSSION

The present study did not demonstrate positive relationship between amount of visible subpapillary plexus and a family history positive for mental illness. This represents a lack of support for an earlier study by Maricq (1963a). The failure to find such a positive relationship in the within-hospital phase of this study may be attributable to the high rate of nonrespondents to the family history questionnaire. This explanation, however, would appear to be negated by the fact that similar results were found in the within-family study in which the parents of the probands were interviewed directly with respect to family history specific for schizophrenia. The over-all results did not indicate a significant relationship between the amount of plexus and a family history positive for schizophrenia. It should be noted that family history data proved to be the most difficult kind of information to obtain in the interviews. Respondents were much more willing to talk about their own psychological difficulties and those of their spouses and children than they were to talk about their own mothers, fathers, and siblings. There was, however, a tendency toward parental predominance favoring the father's side. When the father had the higher plexus, his family tended to show a greater incidence of schizophrenia.

The difficulties in obtaining accurate family history data are probably more pronounced in psychiatric genetics, but have also been proven a serious contaminant in genetic studies of such physical disorders as diabetes (Fuller & Thompson, 1960). Even though extensive contacts were made with the respondents, most of whom showed a very cooperative attitude, marked discrepancies were noted when each spouse was questioned about the history of mental illness in the family. These discrepancies underscore the poor reliability of the interview method for obtaining an accurate picture of familial mental health history.

The nonsignificant correlations between degree of plexus and age of onset, duration of illness, and number and length of hospitalizations do not support the findings of a number of investigators cited previously. There is reason to believe that the findings of the present study are less representative than those of previous investigators, and may be due to factors unique to the hospital population used here. Admission policy at this hospital discriminates against accepting young patients, who would show early onset. The hospital is filled beyond its capacity, and there is also considerable pressure to discharge patients to allow new admissions. This frequently leads to discharge decisions made on the basis of socioeconomic factors unrelated to the course of the illness.

Prognostic predictions are usually made on the parameters listed above. However, Phillips (1953) has demonstrated that sexual and interpersonal adjustments are more efficient predictors. In this study there was a significant correlation between degree of plexus and prognostic morbidity as measured by the Phillips Scale. Consequently, we can say with confidence that there is a relationship between plexus and prognosis. These findings are supported by Maricq (1963a), who found a high plexus group to have marked inadequacies in heterosexual adjustments.

The relationship between plexus and diagnostic categories shows that paranoids have less plexus. This finding supports the studies of Hauptmann and Meyerson (1948) and Wertheimer and Wertheimer (1955). In view of the present study's evidence for heritability of the plexus, it appears that the paranoid form of schizophrenia exhibits less of this genetically controlled constitutional correlate of the disorder. This finding is consonant with the previous studies in psychiatric genetics, which show that there is a lower incidence of schizophrenia in the families of paranoid probands.

Heritability of the plexus is strongly supported by the parent-child comparisons. This finding extends the results of previous research with twins,which show that other aspects of capillary morphology are under genetic control. The finding that the plexus (a distinguishing characteristic of schizophrenia only among the various diagnostic categories of mental illness) is a heritable characteristic provides a somatic sign which will be useful in further investigations of the genetics of schizophrenia.

The establishment of the heritability of the plexus is only the first step, however, and further work remains to be done on the mode of transmission and problems of penetrance. Although the average mid-sibling rating is almost identical with the average mid-parent rating (Table 7), we find that the rating for the average mid-brother is significantly smaller than the average mid-sister rating. This indication of a differential penetrance between males and females may also contribute to the significant difference between fathers and mothers. However, the significant negative correlations between husband and wife on the plexus variable, as shown in Figure 4, raise the question of associative mating in the sample. Concerning factors affecting mate selection, two considerations claim attention. First, the probands have both schizophrenia and a visible plexus. Therefore, to the extent that these traits are inherited, we would expect to find sizable plexus and schizotypy ratings in the parents. If both parents have low schizotypy or plexus ratings, the odds that their children would appear as probands are much reduced. The second consideration is of a different kind. One of the criteria used in selecting the probands was the availability of their families. Another criterion was that the family be intact and reasonably large. However, if both parents are highly schizotypic, neither of these criteria are likely to be met. The chances are small that the family is either intact or large. The children (if any) are not then likely to appear as probands, not because they are not schizophrenic, but because the rest of the family, at least the parents, is scattered.

These two considerations also shed light on the sex difference noted. Male schizophrenics are less fertile than normal males (Meehl, 1962), whereas female schizophrenics have approximately as many children as other women (Kallmann, 1964). From this consideration alone, we would expect to find higher schizotypy ratings among the mothers than among the fathers. Since schizophrenic men have fewer children, a random cut through a population of schizophrenics includes fewer patients with schizophrenic fathers than with schizophrenic mothers. It is also true that a family can sustain schizophrenia more easily in the wife than in the husband. If the husband is schizophrenic, the family is more likely to break up, among other reasons because of reduced income, whereas if the wife is schizophrenic a normal male may be able to maintain the family intact, at least economically.

Both these considerations tend to load this study's population with wives who have higher schizotypy ratings than their husbands. At the same time it also makes for a somewhat special population. In our data, schizophrenia and the visible plexus generally descended from the mother's side, and this fact may have something to do with the higher plexus ratings of the sisters. The plexus rating in general does not appear to be sex-limited; however, in this population, which is loaded to the mother's side, it appears to be. The information on parental predominance, however, casts doubt on the idea that either plexus or schizotypy is sex-limited. When the father was predominant on plexus, it was found that he was predominant on schizotypy. Further, it was also found that, when the father's side of the family was the only one which showed a history of schizophrenia, he was always the predominant parent on the schizotypy ratings. These findings offer no additional information on the general tendency toward maternal predominance, but they do add an unexpected increment of support to the idea that there is a relationship between plexus, schizotypy, and a family history of schizophrenia.

The results of the testing of Hypothesis 4 constitute the central finding of this study. The amount of visible subpapillary plexus is positively related to the amount of schizotypy. As Chapter I showed, the plexus fulfills most of the criteria necessary for participating in the constitutional diathesis in schizophrenia. The results of the present study support the idea that the plexus is a heritable characteristic. The positive correlation between plexus and schizotypy fulfills the requirement implicit in Meehl's theory (1962) that the diathesis must be present prior to the development of the schizophrenic reaction.

It has been shown that the plexus is characteristic of schizophrenia in most of its forms. It has been demonstrated in the present study that the plexus is a heritable characteristic which bears a strong positive relationship to schizotypy. Schizotypy is defined by Meehl (1962) in terms of those behaviors which extend well into the range of subclinical schizophrenia. Consequently, these findings support the proposition that the plexus is a genetically controlled antecedent to the schizophrenic reaction which contributes to the diathesis and is of etiological significance.

It was pointed out in Chapter I that, within Meehl's diathesis-stress theory, it was premature to attempt a sharp distinction between a genetic defect which promotes schizophrenia, and constitutional defenses against its manifestations. Both would contribute in a complementary relationship to form the diathesis. In terms of what is now known about the role of the plexus, it may be possible to speculate more stringently. From the examination of the families' pedigrees regarding plexus, it is clear that no simple Mendelian transmission can account for its prevalence. The closeness of the correlations between the two generations is on the order of those found for polygenic characteristics when environmental factors have been controlled.

There is a direct link between plexus and mesomorphy, and mesomorphy bears a negative relationship to both incidence and severity of schizophrenia. Wertheimer and Wertheimer (1955), in fact, point out that plexus differentiates better than mesomorphy between normals and the various kinds of schizophrenia. It appears that both plexus and mesomorphy are indications of the adequacy of mesodermal development, but that plexus is the more accurate.

It is not surprising that the degree of plexus provides a more sensitive indicator of the adequacy of development of mesodermal structures, because the visibility of the plexus depends on the thickness of the corium. The corium is the mesodermally derived tissue layer from which the vasculature arises during embryonic development. The vascular structures in turn participate in the development of the more gross components of mesomorphy, such as striated muscle. The plexus, then, appears to be heritable, to bear an approximately linear relationship to the degree of schizophrenic psychopathology from mild to severe, and to reflect the inadequacy of mesodermally derived histological structures. In these terms, the plexus appears to measure the mesodermally derived constitutional defense which has been hypothesized by Meehl (1962) and Kallmann (1953).

In future research in the genetics of schizophrenia, it would appear profitable to hypothesize a two-factor theory: first, the gene promoting the disease; second, an independently distributed resistance factor. With plexus controlled both experimentally and statistically, the mode of transmission of the primary genetic defect might be discerned more clearly. At the present, the concept of penetrance has little explanatory power in the genetics of schizophrenia. It is fair to say that the invocation of penetrance has obscured rather than clarified, since there have been no ways to measure penetrance. It is proposed that the degree of plexus might serve as a quantifiable measure of penetrance.

The folding condition observed during this study has been alluded to by Norris and Chowning (1964) and Wertheimer and Wertheimer (1955). Previous researchers did not relate the folding condition to plexus. It has been demonstrated in the present study that plexus does exist in this condition, but is obscured and rendered essentially unquantifiable. The most immediate implication of this finding is that previous assessments of plexus in schizophrenia are an underestimate. The present study does not provide precise measures, but does indicate that the underestimate of plexus in schizophrenia may be around 10 percent.

Folding as a separate condition warrants further study, including histological investigations. Despite the fact that the long history of studies of the nailfold capillaries has emphasized the stable morphology of the capillaries, Maricq (1966) reports two cases of change in plexus which paralleled the clinical course of the disease. In the present study, one case of change in degree of plexus was found. This patient, who was almost a textbook picture of schizophrenia, on first examination showed a 0 (zero) degree of visible plexus but a prominent display of the condition which later was conceptualized as folding. This patient was included with a group who were reexamined 18 months later. In this group of 56 patients, this case was the only one showing any change. The plexus rating had changed from 0 to 4, and clear signs of schizophrenic deterioration were prominent in her behavior. Consequently, it is possible that the folding condition may be related to biological variations within the clinical course of the disease, which are a correlate of outcome.

At the present, some of the relationships between plexus and schizophrenia and plexus and schizotypy are clear, but we do not know in fact whether schizotypes decompensate into schizophrenics. To fill this gap, longitudinal studies of schizotypes must be carried out. If the plexus remains stable, then the precipitating stresses in those schizotypes who do decompensate could be seen more clearly. Within a diathesis-stress theory, precise estimates of the strength of the constitutional aspects should greatly facilitate the study of the relevant psychological factors in the specific etiology of the disorder.

Research on the developmental aspects of the plexus has important implications for the prevention of the schizophrenic reaction. It is known that the plexus is present in all young children and that it disappears rapidly in the first few years of life. Maricq (1965) has shown that by age 15 in a normal population, the plexus has receded almost completely. On the basis of present evidence, it has been assumed that those schizotypes who show plexus are people in whom the plexus has persisted since childhood. It will, however, require longitudinal studies starting prior to adolescence and continuing for a number of years into young adulthood to determine whether this is the case. If research supports the notion that schizotypes are those in which the plexus has persisted from childhood, then a group of people predisposed to schizotypy, and presumably to schizophrenia, have been identified. Most importantly, these people can be identified several years before the usual age of onset of schizophrenia. If identification of predisposed persons could be made in early adolescence, response to psychotherapeutic procedures and environmental manipulation would be maximized.

One further avenue of future research must be pointed out. David (1957) reviewed the histopathology of schizophrenia and concluded that the _Schwundzellen_ (dwarf cells) found by Vogt and Vogt may be the most significant finding in the histopathology of the disorder. They found clusters of dwarf cells in the thalami (_nucleus medialis dorsalis_) of young catatonics. These cell clusters were not found in normals nor in paranoid schizophrenics. David has demonstrated by his own research that such clusters of cells are vascularized by a single arteriole and drained by a single venule: Therefore the cluster of dwarf cells surrounds the capillary itself. Since the dwarf cells are not seen by the Vogts as lesions, but rather as different cell shapes, there may be a similarity between this condition and the inadequate corium which promotes a visible plexus. The appearance of the dwarf cells in catagonics but not in paranoid forms contributes to the possible relevance of the observation. It will be recalled that a visible plexus is much more characteristic of the catatonic than of the paranoid form of schizophrenia. Studies exploring the relationship between plexus and Schwundzellen might provide a link between circulatory anomalies and histopathology in the central nervous system. This notion has special appeal because the function of the dorsomedial nucleus is to integrate somatic and visceral sensory impulses, and to present them to the cortex in a complex form as sensory concepts. The dorsomedial nucleus also has connections with the striatum and may influence the association of sensory and motor activity (Peele, 1961). It is quite possible that the difficulties in these functions of the dorsomedial nucleus appear as the symptoms of disturbances in body schema which are so prominent in schizophrenia.

CHAPTER V

SUMMARY

The central purpose of this study is the evaluation of the relationship between a visible subpapillary plexus in the nailfold and the manifestation of schizophrenic psychopathology within the families of diagnosed schizophrenics. The four major hypotheses primarily generated within the context of a diathesis-stress theory of schizophrenia were:

1. Schizophrenic subjects who have a family history positive for a major mental illness will show a greater amount of subpapillary plexus than schizophrenic subjects with a family history negative for mental illness.

2. In schizophrenic subjects the degree of subpapillary plexus is inversely related to good prognosis.

3. Within-family comparisons spanning at least two generations will demonstrate that a visible plexus is a heritable characteristic.

4. In first-degree relatives of schizophrenic probands there is a positive correlation between amount of subpapillary plexus and schizotypy.

The investigation took place in two parts: an in-hospital study, and a within-family study. There were 164 Ss and a subsample of 50 male Ss utilized in the in-hospital study. These were hospitalized patients diagnosed as schizophrenic. The in-family study used 106 first-degree relatives of 34 probands who were both schizophrenic and showed a visible plexus.

The plexus ratings were made on a four-point scale following microscopic evaluation of the nailfold. Two other ratings were utilized, the Phillips Rating Scale (PRS), a prognostic index, and a Schizotypy Rating Scale. A family history of mental illness was determined by using a questionnaire and personal interview.

Comparisons were made between amount of plexus and several measures of prognosis; plexus and family history; plexus ratings between first-degree relatives and between schizotypy and plexus in the first-degree relatives of the probands.

Hypothesis 1 was not supported. There was no significant variation in plexus as a function of a family history for mental illness.

Hypothesis 2 was supported when the PRS was the dependent measure. The degree of plexus was inversely related to good prognosis. While this finding was significant at the .01 level, age of onset and length of hospitalization (frequent measures of prognosis) were not significantly related to plexus.

Hypothesis 3 was strongly supported. There were nearly identical plexus ratings for the parents and the offspring in the probands' families.

Hypothesis 4, the main concern of this study, was clearly supported. A number of analyses each revealed a significant relationship between plexus and schizotypy.

The following conclusions emerge from the results of this study:

1. The degree of subpapillary plexus is positively related to poor prognosis in schizophrenia.

2. The plexus is a heritable characteristic. The nearly identical plexus ratings of parents and offspring indicate a polygenic mode of transmission.

3. The amount of subpapillary plexus is positively related to the amount of schizotypy.

4. The subpapillary plexus fulfills the major requirements for a constitutional defect participating in the diathesis. Therefore, those mesodermally derived structures within the corium which mitigate against a visible plexus

meet the requirements of a constitutional defense, as postulated by the diathesis-stress theory of schizophrenia.

5. The subpapillary plexus, as a quantifiable contribution to the constitutional diathesis, holds promise as a measure of penetrance in the genetics of schizophrenia.

6. The developmental history of the subpapillary plexus, which characterizes both schizophrenia and schizotypy, shows that in the normal condition the plexus recedes before the age of onset of most of the schizophrenias. If developmental studies show that the plexus persists through adolescence in schizotypes, the plexus may prove to be useful in prior identification of a predisposition for schizophrenia.

APPENDIX A

PHILLIPS PROGNOSTIC RATING SCALE

PHILLIPS PROGNOSTIC RATING SCALE

(MALE FORM)

NAME________________________
AGE__________________________
EDUCATION____________________
RELIGION_____________________

DATE________________________
RATER_______________________
HOSPITAL____________________
SOURCE OF INFO.______________
TOTAL SCORE_____
PREMORBID CLASSIFICATION_____

A. RECENT SEXUAL ADJUSTMENT

1. Stable heterosexual relation and marriage----------0
2. Continued heterosexual relation and marriage but unable to establish home----------------------1
3. Continued heterosexual relation and marriage broken by permanent separation--------------------2
4. (a) Continued heterosexual relation and marriage but with low sexual drive---------------------3
   (b) Continued heterosexual relation with deep emotional meaning but emotionally unable to develop it into marriage-------------------3
5. (a) Casual but continued heterosexual relations, i.e., "affairs," but nothing more--------------4
   (b) Homosexual contacts with lack of or chronic failure in heterosexual experiences------------4
6. (a) Occasional casual heterosexual or homosexual experience with no deep emotional bond---------5
   (b) Solitary masturbation with no active attempt at homosexual or heterosexual experiences------5
7. No sexual interest in either men or women----------6

B. SOCIAL ASPECTS OF SEXUAL LIFE DURING ADOLESCENCE AND IMMEDIATELY BEYOND

1. Always showed a healthy interest in girls with a steady girl friend during adolescence------------0
2. Started taking girls out regularly in adolescence--1
3. Always mixed closely with boys and girls-----------2
4. Consistent deep interest in male attachments with restricted or no interest in girls------------3
5. (a) Casual male attachments with inadequate attempts at adjustment to going out with girls-------------------------------------4
   (b) Casual contacts with boys and girls------------4
6. (a) Casual contacts with boys and with lack of interest in girls--------------------------------5
   (b) Occasional contacts with girls----------------5

7. No desire to be with boys and girls; never went out with girls--------------------------------------6

C. SOCIAL ASPECTS OF RECENT SEXUAL LIFE: 30 YEARS OF AGE AND ABOVE

1. Married and has children, living as a family unit--0
2. Married and has children but unable to establish or maintain a family home---------------------------1
3. Has been married and had children but permanently separated--------------------------------2
4. (a) Married but considerable marital discord-------3
   (b) Single, but has had engagement or deep heterosexual relationship but emotionally unable to carry it through to marriage---------3
5. Single, with short engagements or relationships with women which do not appear to have had much emotional depth for both partners, i.e., "affairs"--4
6. (a) Single, has gone out with a few girls but without other indications of a continuous interest in women-------------------------------5
   (b) Single, consistent deep interest in male attachments, no interest in women--------------5
7. (a) Single, occasional male contacts, no interest in women-------------------------------6
   (b) Single, interested in neither men nor women----6

D. SOCIAL ASPECTS OF RECENT SEXUAL LIFE: BELOW 30 YEARS OF AGE

1. Married, living as family unit, with or without children---0
2. (a) Married, with or without children, but unable to establish or maintain a family home---1
   (b) Single but engaged or in a deep heterosexual relationship (presumably leading toward marriage)--------------------------------------1
3. Single, has had engagement or deep heterosexual relationship but has been emotionally unable to carry it through to marriage-----------------------2
4. Single, consistent deep interest in male attachments, with restricted or lack of interest in women-----------------------------------3
5. Single, casual male relationships with restricted or lack of interest in women----------------------4

6. Single, has gone out with a few girls casually but without other indications of a continuous interest in women------------------------------------5
7. (a) Single, never interested in or never associated with either men or women------------6
   (b) Antisocial------------------------------------6

E. PERSONAL RELATIONS: HISTORY
1. Always has had a number of close friends but did not habitually play a leading role-------------1
2. From adolescence on had a few close friends--------3
3. From adolescence on had a few casual friends-------3
4. From adolescence on stopped having friends---------4
5. (a) No intimate friends after childhood-----------5
   (b) Casual but never any deep intimate mutual friendships----------------------------5
6. Never worried about boys or girls; no desire to be with boys and girls--------------------------6

F. RECENT PREMORBID ADJUSTMENT IN PERSONAL RELATIONS
1. Habitually mixed with others, but not a leader-----1
2. Mixed only with a close friend or group of friends--3
3. No close friends; very few friends; had friends but never quite accepted by them------------------4
4. Quiet; aloof; seclusive; preferred to be by self---5
5. Antisocial--6

APPENDIX B

FAMILY HISTORY

FAMILY HISTORY

Age, sex, diagnosis, onset, number of siblings, family history, number and length of hospitalizations of the 34 probands in the within-family study.

Proband	Age	Sex	Diagnosis	Onset	Sibs.	Family History		Hospitalizations	
						Pat.	Mat.	No.	Length (mos.)
1	34	M	22.3	19	4	. .	. .	4	144
2	21	M	22.3	19	3	. .	. .	2	3
3	30	F	22.5	22	1	U	U	3	46
4	22	M	22.5	21	1	. .	. .	1	2
5	23	F	22.5	21	1	. .	. .	2	13
6	19	M	22.5	19	4	F,A	. .	1	3
7	24	M	22.3	20	1	. .	GM	3	22
8	29	F	22.5	29	2	U	. .	1	2
9	16	M	22.2	15	2	. .	. .	2	4
10	22	M	22.3	20	6	2U	. .	3	12
11	23	F	22.2	22	2	. .	2C	1	4
12	27	M	22.5	24	1	. .	. .	3	22
13	19	M	22.2	19	2	GM	U	1	2
14	17	M	22.2	16	2	U	GM	1	12
15	25	f	22.2	25	1	. .	A	1	3

FAMILY HISTORY--(Continued)

Proband	Age	Sex	Diagnosis	Onset	Sibs.	Family History		Hospitalizations	
						Pat.	Mat.	No.	Length (mos.)
16	20	M	22.2	16	3	. .	M	2	48
17	15	M	22.5	13	10	. .	. .	1	4
18	15	M	22.5	13	4	GA	U	1	4
19	23	M	22.5	22	3	. .	. .	1	8
20	27	M	22.3	26	1	. .	. .	2	14
21	15	M	22.5	15	1	. .	M	1	6
22	25	F	22.3	22	2	. .	M	3	14
23	24	M	22.2	23	2	. .	. .	1	7
24	19	M	22.5	19	3	. .	. .	1	1
25	20	F	22.3	19	2	GM	. .	1	3
26	16	F	22.2	16	2	. .	GM	1	5
27	24	F	22.2	23	1	. .	A	2	5
28	16	F	22.5	15	4	GF	U	1	4
29	23	F	22.5	23	3	. .	. .	1	7
30	19	F	22.3	19	3	. .	. .	1	2
31	30	F	22.3	20	2	. .	. .	3	47
32	21	F	22.3	19	3	. .	. .	2	4

FAMILY HISTORY--(Continued)

Proband	Age	Sex	Diagnosis	Onset	Sibs.	Family History		Hospitalizations	
						Pat.	Mat.	No.	Length (mos.)
33	17	F	22.2	16	3	. .	. .	2	5
34	17	F	22.5	17	3	F,U	. .	1	1

APPENDIX C

WITHIN-FAMILY INFORMATION

WITHIN-FAMILY INFORMATION

Age, schizotypy rating, plexus rating, and folding in the 34 probands, their parents, and their siblings in the within-family study.

Proband	Relative	Age	Schizotypy	Plexus	Folding
1	Self	34	S	3.5	0
	Father	56	28	3.0	0
	Mother	54	8	1.5	0
	Sister	26	14	0.5	+
2	Self	21	S	2.5	0
	Father	54	0	0.0	0
	Mother	46	8	2.5	0
	Sister	26	14	3.5	0
	Sister	24	12	2.0	+
3	Self	30	S	3.0	0
	Father	53	0	0.0	0
	Mother	53	41	2.5	0
4	Self	22	S	2.0	0
	Father	60	1	0.0	0
	Mother	49	6	2.0	0
5	Self	23	S	2.0	0
	Father	52	16	1.5	0
	Mother	52	9	2.5	0
6	Self	19	S	4.0	0
	Father	46	S	3.0	0
	Mother	47	0	1.5	0
	Sister	21	0	2.5	0
	Brother	17	6	0.5	+
	Sister	15	0	2.5	0
7	Self	24	S	4.0	0
	Father	49	12	3.0	0
	Mother	52	4	1.5	0

WITHIN-FAMILY INFORMATION--(Continued)

Proband	Relative	Age	Schizotypy	Plexus	Folding
8	Self	29	S	3.5	0
	Father	62	16	2.0	0
	Mother	56	13	2.5	0
9	Self	16	S	4.0	0
	Father	44	0	0.0	0
	Mother	42	9	2.5	0
	Sister	17	12	2.5	0
10	Self	22	S	4.0	0
	Father	57	22	0.0	+
	Mother	52	14	3.5	0
	Brother	21	8	2.5	0
	Sister	20	5	2.5	0
	Sister	19	12	3.0	0
11	Self	23	S	3.5	0
	Father	48	0	1.0	0
	Mother	49	14	3.5	0
	Brother	28	3	1.5	0
12	Self	27	S	2.0	0
	Father	54	0	0.0	++
	Mother	54	4	0.0	+
13	Self	19	S	3.5	0
	Father	44	5	4.0	0
	Mother	44	0	0.0	0
	Sister	18	3	3.0	0
14	Self	17	S	4.0	0
	Father	42	23	4.0	0
	Mother	39	2	2.0	0
	Sister	15	0	3.5	0
15	Self	25	S	4.0	0
	Father	48	0	0.0	0
	Mother	46	15	3.0	0

WITHIN-FAMILY INFORMATION--(*Continued*)

Proband	Relative	Age	Schizotypy	Plexus	Folding
16	Self	20	S	4.0	0
	Father	45	0	0.0	0
	Mother	42	S	2.0	0
17	Self	15	S	3.0	0
	Mother	50	30	0.0	0
	Sister	34	22	4.0	0
	Sister	28	0	0.0	0
	Sister	25	4	3.0	0
	Sister	23	8	0.5	0
	Sister	19	17	2.0	0
18	Self	15	S	3.5	0
	Father	61	11	2.0	0
	Mother	62	26	2.5	0
	Brother[a]	23	22	2.0	0
	Brother[a]	23	18	1.5	0
	Brother	19	0	1.5	0
19	Self	23	S	4.0	0
	Father	45	0	0.0	0
	Mother	46	18	2.5	0
	Brother	16	14	0.0	+
20	Self	27	S	1.0	0
	Father	61	0	0.0	0
	Mother	59	10	3.0	0
21	Self	15	S	4.0	0
	Father	40	7	2.5	0
	Mother	38	S	3.5	0
22	Self	25	S	2.0	0
	Father	51	0	0.0	0
	Mother	49	S	1.5	0
	Sister	22	0	0.0	0

---

[a] Identical twins.

WITHIN-FAMILY INFORMATION--(Continued)

Proband	Relative	Age	Schizotypy	Plexus	Folding
23	Self	24	S	2.5	0
	Father	53	0	0.0	0
	Mother	46	5	2.5	0
24	Self	19	S	4.0	0
	Mother	44	11	2.5	0
	Sister	24	26	3.0	0
	Sister	17	3	1.5	0
25	Self	20	S	3.0	0
	Father	45	5	4.0	0
	Mother	45	0	0.0	0
	Brother	17	0	3.0	0
26	Self	16	S	3.0	0
	Father	44	26	4.0	0
	Mother	41	6	2.0	0
27	Self	24	S	4.0	0
	Father	49	0	0.0	0
	Mother	49	15	3.0	0
28	Self	16	S	3.0	0
	Father	62	12	2.0	0
	Mother	60	24	2.5	0
	Brother	24	21	2.0	0
	Brother	23	17	1.5	0
	Sister	18	0	1.5	0
29	Self	23	S	3.0	0
	Father	45	0	0.0	0
	Mother	48	18	2.5	0
	Sister	19	4	0.0	+
30	Self	19	S	3.5	0
	Father	48	0	0.0	0
	Mother	47	13	2.5	0
	Sister	22	26	3.0	0
	Sister	18	3	1.5	0

WITHIN-FAMILY INFORMATION--(Continued)

Proband	Relative	Age	Schizotypy	Plexus	Folding
31	Self	30	S	3.0	0
	Father	60	29	3.0	0
	Mother	58	8	1.5	0
	Brother	28	12	0.5	0
32	Self	21	S	3.0	0
	Father	54	0	0.0	0
	Mother	47	9	2.5	0
	Sister	25	14	3.5	0
	Sister	24	13	2.0	0
33	Self	17	S	4.0	0
	Father	43	0	0.0	0
	Mother	43	9	2.5	0
	Sister	18	13	2.5	0
	Brother	15	0	0.0	0
34	Self	17	S	4.0	0
	Father	51	S	3.0	0
	Mother	49	0	1.5	0
	Brother	22	0	2.5	0
	Sister	19	10	3.5	0
	Sister	15	0	2.5	0

APPENDIX D

SCHIZOTYPE CHECK LIST WITH SCORE WEIGHTING

SCHIZOTYPE CHECK LIST WITH SCORE WEIGHTING

Name__________________________Sex____No._______Date_________

Rater_____________________Hours contact_____D_x_____________

Check (X) those symptoms or traits which you are highly confident are present, and in the degree implied by the phrase and its modifiers. Thus, if "Ambivalence" is present, but is not clearly "intense," this sign should not be checked. Scoring, weighting, cutting, and validation are based on such strict rating instructions. Whatever your views about the diagnostic meaning of these signs, please try to set all such thoughts aside, judging each item "by itself" as objectively as possible.

1. __1__Ambivalence, intense
2. __3__Anhedonia (pleasure-deficit)
3. __3__Body-image aberrations
4. __1__Chaotic sexuality
5. __3__Cognitive slippage
6. __1__Countertransference strain on you
7. __1__Deflated self-esteem: Severe + inappropriate + diffuse
8. __3__Dependency, demandingness
9. __2__"Different from others" feeling explicitly stated
10. __2__Distrust, testing operations, closeness-panic
11. __1__Failure to achieve, gross (Corrected for capacity)
12. __2__Flat or spotty affectivity
13. __1__Hatred of mother, manifest, expressed
14. __2__Magical ideation or action

15. 6 Micropsychotic episodes (include "drift-outs" in interview)

16. 1 Narcissism, extreme

17. 1 Pan-anxiety

18. 1 Poor outcome (include clearly premature termination)

19. 11 Psychosomatic or neurological signs

20. 2 Rage: intense, phenotypic, verbalized, disproportionate

21. 12 Repetition of material

22. 1 Self-injury (physical, social, professional, sexual)

23. 1 Social fear (include marked preference to "be alone")

24. 2 Special signs

25. 2 Suicidal (attempt, or dread, or chronic "thoughts")

w_c= 46 possible

REFERENCES

Ash, P. The reliability of psychiatric diagnosis. Journal of Abnormal and Social Psychology, 1949, 44, 272-276.

Bellak, L. (Ed.) Schizophrenia: a review of the syndrome. New York: Logos Press, 1958.

Bleuler, E. Dementia praecox. New York: International Universities Press, 1911.

Cobb, S., & Fremont-Smith, F. The cerebral circulation. XVI. Changes in the human retinal circulation and in the pressure of the cerebral spinal fluid during inhalation of a mixture of carbon dioxide and oxygen. Archives of Neurology and Psychiatry, 1931, 26, 731-736.

Connolly, C. J. Physique in relation to psychosis. Studies in psychology and psychiatry. Catholic University of America, No. 5, 1939.

Cumming, J. The family and mental disorder: an incomplete essay. Milbank Memorial Educational Quarterly, 1961, 39, 185.

David, G. B. The pathological anatomy of the schizophrenias. In D. R. Richter (Ed.), Schizophrenia: somatic aspects. New York: Pergamon Press, 1957, pp. 93-130.

Davidson, C. M. Schizophrenia: a survey of theory and practice. Journal of Mental Disorders, 1956, 123, 149-161.

Filipini, C. A. Hypothesis on schizophrenia. Rassegna Di Studi Psichiatrici, 1947, 36, 296-309.

Fuller, J. L., & Thompson, R. W. Behavior genetics. New York: Wiley, 1960.

Hauptmann, A., & Meyerson, A. Studies of finger capillaries in schizophrenia and manic depressive psychoses. Journal of Nervous and Mental Diseases, 1948, 108, 91-108.

Hurst, L. A. Genetics of schizophrenia. Psychological Bulletin, 1951, 48, 402-412.

Hurst, L. A. Genetics of schizophrenia. Psychological Bulletin, 1952, 49, 544-546.

Jaensch, W. Die hautkapillaroskopie. Halle: Carl Marhold, 1929.

Kallmann, F. J. Genetic theory of schizophrenia. American Journal of Psychiatry, 1946, 103, 309-322.

Kallmann, F. J. Heredity in health and mental disorder. New York: Norton, 1953.

Kallmann, F. J. The developmental aspects of children with two schizophrenic patients. In Philip Solomon and Bernard C. Glueck (Eds.), Recent research on schizophrenia. Washington, D.C.: American Psychiatric Association, 1964, pp. 136-145.

Kallmann, F. J., & Barrera, S. E. The heredo-constitutional mechanisms of predisposition and resistance to schizophrenia. American Journal of Psychiatry, 1942, 98, 544-550.

Karlsson, J. L. The biologic basis of schizophrenia. Springfield, Illinois: Charles C Thomas, 1966.

Kety, S. S. Methods in medical research. Chicago: I. Yearbook Publishers, 1948.

Kretschmer, E. Physique and character. London: Kegan Paul, Trench, Trubner, 1925.

Kringlin, E. Schizophrenia in twins. Psychiatry, 1966, 122, 809-818.

Krogh, A. The anatomy and physiology of capillaries. New Haven: Yale University Press, 1929.

Lehmann, W., & Hartlieb, J. Capillaren bei zwillingen. Zeitschrift für menschliche vererbungs und konstitutions-lehre, 1938, 21, 271-285.

Lewis, N. D. C. Constitutional factors in dementia praecox, with particular attention to the circulatory system and to some of the endocrine glands. Nervous and Mental Disease Monograph, 35, Washington, D.C.: Nervous and Mental Disease Monograph Publishing Company, 1923.

Lewis, T. The blood vessels of the human skin and their responses. London: Shaw and Son, 1927.

Lovett-Doust, J. W. Capillary microscopy in psychiatry. In G. W. Fleming (Ed.), Recent progress in psychiatry. London: Journal of Mental Science, 1950, pp. 1-25.

Lovett-Doust, J. W. The capillary system in patients with psychiatric disorders: diminished capillary resistance as shown by Gothlin positive pressure test. Journal of Clinical and Experimental Psychopathology, 1955, 16, 272-280.

Maricq, H. R. Capillary pattern in familial schizophrenics. Circulation, 1963a, March, 406-413.

Maricq, H. R. Familial schizophrenia as defined by nailfold capillary pattern and selected psychiatric traits. Journal of Nervous and Mental Diseases, 1963b, 136, 216-226.

Maricq, H. R. Nailfold capillaries in normal children. Journal of Nervous and Mental Diseases, 1965, 141, 197-203.

Maricq, H. R. Capillary morphology and the course of illness in schizophrenic patients. Journal of Nervous and Mental Diseases, 1966, 142, 63-71.

Mauz, F. Die prognostic der ergogensen psychosen. Leipzig: Thieme, 1930.

Meehl, P. E. Schizotaxia, schizotypy, schizophrenia. *American Psychologist*, 1962, *17*, 827-838.

Meehl, P. E. *Manual for use with check list of schizotypic signs*. Unpublished manuscript, Psychiatric Research Unit, University of Minnesota Medical School, Minneapolis, Minnesota, copyright, 1964.

Muller,O. *Die cappillaren der menschlichen kroperoberfläche in gesunden und kranken tagen*. Stuttgart: Ferdinand Enke, 1922.

Norris, A. S., & Chowning, J. R. Capillary morphology of the nailfold in the mentally ill. *Journal of Neuropsychiatry*, 1964, *5*, 225-234.

Osato, S., & Awano, I. Genetische studien an zwillingen. *Morphologischer Tell. A. Ge. Me. Ge.*, 1957, *6*, 283-366.

Pastore, N. The genetics of schizophrenia. *Psychological Bulletin*, 1949, *46*, 285-302.

Peele, T. L. *The neuroanatomic bases for clinical neurology*. 2nd ed., New York: McGraw-Hill, 1961.

Phillips, L. Case history data and prognosis in schizophrenia. *Journal of Nervous and Mental Diseases*, 1953, *117*, 515-525.

Planansky, K. Heredity in schizophrenia. *Journal of Nervous and Mental Diseases*, 1955, *122*, 121-142.

Rees, L. Physical characteristics of the schizophrenic patient. In D. Richter (Ed.), *Schizophrenia: somatic aspects*. New York: Pergamon Press, 1957, pp. 1-14.

Richter, D. (Ed.) *Schizophrenia: somatic aspects*. New York: Pergamon Press, 1957.

Rosenthal, D. Some factors associated with concordance and discordance with respect to schizophrenia in monozygotic twins. *Journal of Nervous and Mental Diseases*, 1959, *129*, 1.

Rosenthal, D. Sex distribution and the severity of illness among samples of schizophrenic twins. Journal of Psychiatric Research, 1961, 1, 26-36.

Rosenthal, D. Familial concordance by sex with respect to schizophrenia. Psychology Bulletin, 1962, 59, 401-421.

Rosenthal, D. (Ed.) The Genain quadruplets. New York: Basic Books, 1963, 505-511.

Sandifer, M. G.; Pettus, C.; & Quade, D. A study of psychiatric diagnosis. Journal of Nervous and Mental Diseases, 1964, 139, 350-356.

Schiller, M. Zwillingsprobleme. Zeitschrift für menschliche vererbungs-und konstitutions-lehre, 1937, 20, 285-337.

Serota, H. Temperature changes in the cortex and hypothalamus during sleep. Journal of Neurophysiology, 1939, 2, 42-47.

Shattock, F. M. The somatic manifestations of schizophrenia: a clinical study of their significance. Journal of Mental Science, 1950, 96, 32-142.

Sheldon, W. H. The varieties of human physique. New York: Harper, 1940.

Siegel, S. Nonparametric statistics for the behavioral sciences. New York: McGraw-Hill, 1956.

Spalteholz, W. Blulge fässe der hant-und geschlechtskrank heiten. In J. Jadassohn, Handbuch der hant and geschlechtskrankheiten, I. Berlin: Julius Springer, 1927.

Srole, L. Mental health in the metropolis: the midtown Manhattan study, I. New York: McGraw-Hill, 1962.

Tienari, P. Psychiatric illnesses in identical twins. Acta Psychiatrica Scandia, 1963, 39, 9-195 (Suppl. 171).

Tsung-Yi Lin, & Standley, C. C. *The scope of epidemiology in psychiatry*. Geneva: World Health Organization, 1962.

Wertheimer, N., & Wertheimer, M. Capillary structure: its relation to psychiatric diagnosis and morphology. *Journal of Nervous and Mental Diseases*, 1955, *121*, 14-27.

Wolff, H., & Lennox, W. The cerebral circulation. XII. The effect on pial vessels of variation in the oxygen and carbon dioxide content of the blood. *Archives of Neurology and Psychiatry*, 1930, *23*, 1097-1120.

BIOGRAPHICAL SKETCH

Charles Edward Buchanan was born in Somerset, Kentucky, on May 17, 1928. In August, 1950, he received the Bachelor of Arts degree with a major in psychology from Duke University. From 1951 to 1955 he attended the University of Kansas and did graduate work in psychology. During this time he spent two years as a Veterans Administration trainee in clinical psychology. During 1955 and 1956 he completed internship in the Menninger Clinic-Topeka State Hospital Psychology Training Program. He held the position of Staff Psychologist at Topeka State Hospital during 1957 and 1958. From 1959 through 1961 he held the position of Research Associate, Department of Psychiatry, University of Florida. In 1962 he returned to full-time graduate study at the University of Florida and held a Fellowship in Rehabilitation Counseling. From 1966 to 1968 he held the position of Director of Psychology at the North East Florida State Hospital. His publications include:

(with J. L. Dowis) Some relationships between intellectual efficiency and the severity of psychiatric illness. J. of Psychol., 1961, 51, 371-381.

The rehabilitation of the hysterectomy patient. J. Rehab., March-April, 1963, 29, 17.

This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of that committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council, and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

June, 1968

E. Ruffin Jones
Dean, College of Arts and Sciences

Dean, Graduate School

Supervisory Committee

Marshall B. Jones
Chairman

Charles J. Hunt Jr.

Louis D. Cohen

Bruce Thomas

Richard J. Anderson